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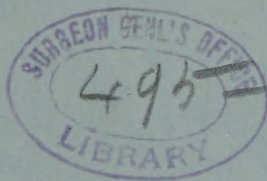
TUBERCULOSIS OF THE ŒSOPHAGUS.

(LARVÆ OF DIPTERA IN THE ULCERS.)

BY SIMON FLEXNER, M. D., *Associate in Pathology.*

[From the Pathological Laboratory of the Johns Hopkins University and  
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presented by the author.





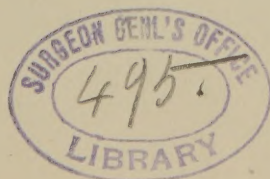
# TUBERCULOSIS OF THE ŒSOPHAGUS.

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Among those organs which writers on tuberculosis have considered as relatively if not absolutely immune the œsophagus occupies a prominent place. Indeed, until recent years, well authenticated examples of tuberculosis of the œsophagus are not met with in the literature, so that Zenker, writing in V. Ziemssen's Handbook in 1876, still considers the question whether tuberculosis occurs in this organ an open one, and one searches the older pathological anatomies in vain for a reference to this subject. Rokitsansky states in his pathological anatomy that tuberculous deposits are rarely, if ever, found in the œsophagus, and that they must not be confounded with the tubercular degeneration of the neighboring lymphatic glands. Hence, while this author does not entirely exclude the possibility of tuberculous processes beginning in the œsophagus, it must be inferred that he did not know of an undoubted case. It is only within the last ten years, since the articles of Weichselbaum and Beck appeared, that this affection has secured a place in the literature of tuberculosis, although a few isolated examples of the disease had been recorded before. Yet in the earlier cases, with a few exceptions, entirely satisfactory evidence of the tuberculous nature of the process in the œsophagus was not given, and Weichselbaum was therefore inclined to exclude all these from the list of tuberculous affections of the œsophagus. In this way he rejected the cases reported by Paulicki, Chovstek, Zenker and V. Ziemssen and Breus, the only ones with which he was acquainted save his own. Beck agreed with Weichselbaum in reference to all these excepting that of Breus, and





referred to a case reported by Eppinger which escaped the attention of Weichselbaum, which he accepted as tuberculous. Yet both of these authors overlooked the case of Spillman published in 1878, and especially that of Frerichs, reported in 1882, in both of which the lesions doubtless were tuberculous in nature.

In considering the cases of tuberculosis of the œsophagus which have thus far been reported and in which the evidence of the tuberculous character of the affection is satisfactory, it is necessary to distinguish several classes. The first class will embrace those instances in which the tuberculous process arose through continuity or contiguity of structure, as, for example, where a caseous bronchial gland or group of caseous glands become united by inflammatory adhesion to the œsophagus and ulcerated into the latter, or in consequence of perforation of abscesses associated with caries of the vertebræ, and, finally, instances of tuberculous ulcers of the pharynx which, passing downwards, invaded the œsophagus.

Another group can be distinguished on account of the existence in the œsophageal mucous membrane of a previous lesion which is to be regarded as predisposing to the tuberculous infection. Such examples are afforded by the case of Breus and that of Eppinger.

Manifestly such instances as the preceding do not belong in the same category with cases in which the affection of the œsophagus occurred in the course of a general infection of the body with tubercle bacilli in acute disseminated miliary tuberculosis, or the infection of the mucous membrane with tuberculous sputum where no previous predisposing lesion was present.

It cannot be doubted that the œsophagus possesses a marked resistance to invasion with tubercle bacilli, applied either directly to its mucous membrane in cases of lung tuberculosis where the sputum is swallowed, or brought to it by the blood current in the general diffusion of the virus. But the opinion expressed by Eppinger that a previous lesion of the mucous membrane is essential to the development of the process cannot at this time be accepted, although we may be unable to say what the conditions are which determine the occurrence of tubercles at one time and not at another.

To the first class of cases belong those of Weichselbaum,

Beck, Pitt, Penzoldt, Orth\* and Zenker. Weichselbaum reports the case of a woman, aged 36, who had general tuberculous enlargement and caseation of the glands of the neck. The autopsy showed the cervical and mediastinal glands to be caseous; moderate lung tuberculosis, and intestinal tuberculosis. Moreover, four fingers' breadth above the bifurcation of the trachea the posterior wall of the trachea and the anterior wall of the œsophagus presented a perforated and sieve-like appearance. The perforations, which were of the size of a hemp-seed and eight in number, communicated with adjacent caseous lymphatic glands. The mucous membrane and submucous coat of the œsophagus above the perforations contained a few nodules varying in size from a hemp-seed to a pea; but below the perforations the nodules were more numerous. The smaller ones were gray in color, the larger yellow and caseous. The nodules stopped abruptly at the cardiac orifice of the stomach, and the pharynx was free from ulceration. There were, however, ulcers in the trachea and larynx. Histological examination of the ulcers in the œsophagus exhibited a base of granulation tissue on the surface of which necrotic and caseous material were present, and in the caseous material tubercle bacilli were found. The nodules were composed of lymphoid and epithelioid cells and showed, often, central caseation.

The first of Beck's cases occurred in a man of 45. The autopsy showed pyo-pneumo-thorax of the right side with great thickening of the pleura, and in the thickened pleura caseous masses were contained; tuberculous meningitis; in the left hemisphere of the cerebellum a caseous nodule the size of a nut; caseous area in the apex of the left lung; caseation of bronchial and mediastinal glands; large tuberculous ulcers in larynx; large tuberculous ulcer in posterior wall of trachea, miliary tubercles in trachea below the ulcer and in the right bronchus. The œsophagus contained in its anterior wall, opposite the bifurcation of the trachea, a diverticulum which appeared to be due to traction exercised by a packet of adherent caseous bronchial glands. At the

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\*Orth states that he has observed three cases, but he describes only two of these with sufficient minuteness to enable them to be classified.



line of junction of the middle and upper third of the œsophagus, on its anterior surface, there was a linear ulcer 3 cm. long by 1 cm. wide. Surrounding the ulcer, which had undermined the mucous membrane, there were fine nodules in the mucous membrane, some of which exhibited a superficial loss of substance. Between the anterior wall of the œsophagus and the posterior wall of the trachea, corresponding with the situation of the ulcer in the former, a spindle-shaped mass of five lymphatic glands was intimately adherent to the œsophagus, and the œsophageal ulcer corresponded with a softened area in the glands. Examination of the ulcer proved it to be tuberculous, and tubercle bacilli were demonstrated in it.

The second one was a laborer of 54, who, three months before his death, complained of difficulty in swallowing. At the autopsy he exhibited slaty induration of the lungs with caseation. In the pons Varolii there was a single caseous tubercle the size of a cherry seed; tuberculous ulcers were present in the larynx and on both sides of the epiglottis. The pharynx was the seat of extensive ulceration, the upper part alone showing a covering of epithelium. The pharyngo-laryngeal portion of the pharynx, the base of the tongue and the upper part of the œsophagus were included in a circular ulceration which was continuous with that described in the larynx and epiglottis. The ulceration in some places extended to the muscular coat; and corresponding with the upper part of the œsophagus, the tissues were dense and hard, owing to the cicatricial contraction, converting this portion into a narrow, rigid tube. Below the ulcer numerous miliary tubercles were to be seen, but they became less in number and finally disappeared as the middle of the œsophagus was approached. These small tubercles were covered with normal epithelium.

Pitt described a case in which adhesion had taken place between the œsophagus and bronchial glands resulting in perforation. Orth has seen two cases, perforation occurring in one in consequence of softened lymph glands, and ulceration in the other from the descent of a pharyngeal tuberculous ulcer.

Zenker saw two cases of extensive secondary perforation of the œsophagus produced by softening of caseous bronchial glands. In one case there was found, in addition, a severe phlegmonous inflammation of the œsophagus, extending the entire length of the tube, which he regards as certainly excited

by the perforation. In the other case the mucous membrane around the perforation, for a distance of 3 cm., was thickly studded with small, round ulcers, extending only as far as the submucous tissue.

The three cases reported by Penzoldt comprise the most reliable literature in the remaining form of this class, namely, perforation of the œsophagus due to caries of the vertebræ. The first occurred in a man of 56, who, at the autopsy, was found to have lung and intestinal tuberculosis, and caries of the 5th and 6th cervical vertebræ. Opposite to the 5th vertebra the posterior wall of the œsophagus was perforated by direct extension of the abscess connected with the diseased vertebræ. In the second case there was caries of the first four dorsal vertebræ in a man of 46, and the œsophagus was perforated, the ulcer measuring 1 cm. in diameter. The finger introduced into the œsophagus could be passed into the cavity of the abscess. The third one relates to a man 53 years old. A partial autopsy only was permitted, and besides old lung tuberculosis, caries was present in the first four dorsal vertebræ. Opposite the first dorsal vertebra an opening 7 mm. in diameter existed in the œsophagus, which was continuous with a cavity in the vertebræ leading into the spinal canal. It must be stated that had histological examinations been made in these cases of Penzoldt, the evidence of the tuberculous nature of the processes would, to say the least, have been more conclusive.

To the second class belong the cases of Breus and Eppinger already alluded to. In the case reported by the former a tuberculous patient swallowed a caustic alkali for suicidal purposes and suffered stricture of the œsophagus in consequence. The autopsy revealed chronic tuberculosis of the lungs and lymph glands; tuberculous ulcers in the intestine; tubercles in the liver, spleen and kidneys. Moreover, there was great constriction of the œsophagus, and its inner surface presented numerous cicatrices and many irregular losses of substance. These ulcers showed in their bases and margins miliary and larger gray and caseous tubercles. There were scars and ulcers in the pharynx and in the stomach also. While no bacteriological examination was made, yet the histological examination showed the ulcers and nodules to be composed of lymphoid and giant cells.



Eppinger's case was a woman, age 45, who suffered from stricture of the œsophagus due to the thrush fungus. At the autopsy the fungus masses were carefully washed away, exhibiting the mucous membrane of the œsophagus covered with tuberculous ulcers varying in size from a pin's head to a pea. These were isolated or in groups. Lung tuberculosis with cavity formation was present and thrush occurred in the trachea. Eppinger states that tuberculosis of the œsophagus does not occur unless there has been a previous pathological change in the mucous membrane to enable the bacilli to enter the tissues. In this instance he believes that the *Oidium* (*Saccharomyces*) *albicans* paved the way for the tuberculous infection.

When the foregoing cases are eliminated, the number of instances which remain in which the infection of the œsophagus may be regarded as occurring under the same conditions as, for example, intestinal tuberculosis, is not large and entirely warrants the conclusion that this structure is relatively, although not absolutely, immune to tuberculous disease. The following instances comprise the third class:

Spillman's case occurred in a man of 51 who had suffered from stricture of the œsophagus, the autopsy revealing an ulcer  $1 \times 1.5$  cm. occupying the middle part of the œsophagus; in the center of which a small, hardly-perceptible perforation communicating with the left bronchus was present. There was pleural tuberculosis. The bronchial glands were swollen and pigmented.

Frerichs studied 30 cases of acute and 250 cases of chronic tuberculosis. In the first series, eight cases had tuberculosis of the pharynx, tonsils or tongue, but in no instance was there œsophageal tuberculosis. Of the chronic cases he found œsophageal tuberculosis in only one case. This was in a child eight years of age who had caseous foci in the lungs, tuberculous ulcers in the pharynx and intestines, and caseous masses in the kidneys. In the lower third of the œsophagus there were several exquisite tuberculous ulcers. The edges of the ulcers were sharp, while the bases had a grayish-yellow appearance and contained caseous detritus. Distinct tubercle nodules were visible in the periphery of the ulcers seated in the intact mucous membrane.



Mazzotti reports three cases belonging to this group. The first in a child of 10 years who died of acute miliary tuberculosis, following tuberculosis of the bronchial glands, in the course of which an eruption of miliary tubercles had taken place in the œsophagus. The second in a man of 39 with cavities in the lungs. Tubercles were present in the depth of the mucous membrane in the upper part of the œsophagus, while lower down ulceration had occurred. The last one was a woman, aged 37, who had lung tuberculosis with cavity formation and intestinal tuberculosis. In the anterior wall of the œsophagus, opposite the larynx, a prominent ring-like elevation the size of a penny was found. This was white in color, opaque and ulcerated. Below the ulcer, 10 or 12 granular elevations no larger than pin-points were seen. In all these cases tubercle bacilli were demonstrated. In none of Mazzotti's cases did the number of ulcers exceed six, and they lay in the lower part of the tube and conformed to its long axis.

To this last class of cases we are enabled to add one. There has been only one reported up to the present time in which a tuberculous ulcer beginning in the œsophagus perforated this tube. We refer to the case of Spillman. In the instance which we observed the perforation took place into the left pleural cavity; and, although it may be anticipating our report, it may be stated here that the tuberculous pleurisy is to be attributed not to an infection of the pleura following this perforation, but to the lung tuberculosis with which it was associated.

\* A woman, A. K., white, aged 33, was admitted on August 3d, 1892, into the medical wards, service of Dr. Osler, of the Johns Hopkins Hospital. When admitted, she complained of cough, fever and shortness of breath. She gave a tuberculous family history, but personally she had always been strong up to Christmas, 1891. Early in 1892, as she stated, she had two attacks of influenza, from which time she dates her present illness. This latter began with cough, which continued from this time on, and in May, 1892, she experienced a sudden and severe pain in the left side. At the St. Joseph's Hospital, whither she went and remained seven weeks, her chest was aspirated once.

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\* The clinical history is taken from the medical and surgical records of the Hospital, by the kind consent of Drs. Osler and Finney.

*Status præsens.* Emaciated, pale; pulse 92 to the minute, compressible, regular in force and rhythm. The left side of the chest bulges and the intercostal spaces are obliterated. The cardiac pulsation is observed in the 2d, 3d and 4th spaces on the right side. Percussion note on the right side clear, except over area of cardiac dulness. On the left side the front note is feeble and tympanitic. The pulmonary resonance ends at lower border of 6th rib in the mammary line on right side; flatness begins on left in line following 6th rib into axilla. In erect posture, on the left side, flatness extends as high as the 3d rib, and posteriorly there is flatness at a point 3 cm. above the angle of the scapula. On this side, behind, there is a fluctuating area 7 cm. in diameter opposite the 8th and 9th spaces, which pulsates with the respirations. Respirations on right side clear; on left enfeebled, and, passing into the flat area, they become distant and tubular. Vocal fremitus absent over the flat area. Over front of left lung, in recumbent position, although respiration is not typically amphoric, there is distinct metallic tinkling; succussion marked. Other viscera negative. Sputum contains tubercle bacilli. The patient was transferred on August 6th, 1892, to the surgical ward for operation.

She was operated upon by Dr. Finney, on the 6th of June, under ether narcosis, and five cm. of the 6th rib excised. Pus did not begin to flow immediately, as the pleural cavity contained air; and the odor emitted was very offensive. Turning the patient on the side, a moderate quantity of dirty grayish pus escaped. While coming from under the ether the patient vomited, and the material ejected had much the appearance of the contents of the pleural cavity. The patient did well after the operation, and on the 10th the following note was made: "The pleural cavity is irrigated daily with normal salt solution, and the washings contain coagulated milk and have a strong odor of whisky, these having been administered by the mouth." On August 18th another note to this effect was made: "Irrigation continued. The patient is now allowed light diet. Small masses of food ingested appear in the washings from the pleural cavity. The wound gapes widely, the diaphragm can be seen moving up and down and the pulsation of the heart can be watched, and by introducing the finger through the wound, felt. Patient is very weak and emaciated;

there is marked but not very severe dyspnoea." August 23d, at 4 P. M., she died.

Autopsy, August 24th, at 8.30 A. M. Anatomical diagnosis: Tuberculosis of lungs, lymph glands of neck and bronchial glands; tuberculous pleurisy; pyo-pneumo-thorax; gangrene of pleura; perforating tuberculous ulcer of œsophagus; intestinal tuberculosis (recent). In reporting the autopsy only such parts of it will be given as bear on the present paper.

*Thorax.* In the left pleural cavity are 500 cc. of a turbid, foul-smelling fluid in which float flakes and coagula mostly white in color; and thick, yellow, sticky pus adheres in places to the walls of the cavity. Both leaves of the pleura are thickened, dark in color and gangrenous in appearance. Small hemorrhagic spots are scattered over the surfaces of the pleura. The lung is much reduced in volume, deeply pigmented and very dense. 3.5 cm. from the posterior border and about midway of the compressed lung is a small opening in the pleura through which a probe can be passed into the lung substance. On section this orifice is seen to lead into a small cavity, the walls of which are composed of a grayish-white, granular, caseous-looking material. The lung is airless, dense, deeply pigmented, and in the lower lobe a number of dilated bronchi filled with thick, purulent material occur. Right lung: free from adhesions; pleura generally delicate. The surface of the lung is moderately pigmented and to the touch has an irregular feel. There are several circumscribed deposits of granular fibrin in the pleura over the lung. On section the consistence of the tissue is increased; the cut surface presents an irregular mottled red and gray color, with other areas deeper red in color, due either to great congestion or hemorrhage. The irregularity of the surface is due to lobular areas of consolidation of the lung substance corresponding with the fresh fibrinous deposits on the surface. In the apex of the lung is a small tuberculous cavity with thick caseous walls which communicates freely with a bronchus.

*Esophagus.* For a distance of 4.5 cm. the œsophagus lies freely exposed in the left pleural cavity. At a point 2.5 cm. above the arch of the aorta where the left common carotid is given off, there is a perforation leading directly into the lumen of the œsophagus. The tissues surrounding the œsophagus are œdematous and hyperæmic, and a considerable



loss of substance has occurred in the connective tissue covering it. For a space of  $4 \times 2$  cm. the connective tissue sheath is entirely wanting or very thin. On section of the œsophagus there are, in the anterior wall, but somewhat to the left of the middle line, two ulcers about equal in size and measuring  $7.5$  by  $4$  mm. The more superficial one reaches the muscular coat but does not penetrate beyond, while the other has perforated the œsophagus and communicates by a small opening with the left pleural cavity. The edges and bases of the ulcers are smooth. In the ulcers are several maggots, still living. Species not determined.

*Lymphatic Glands.* All the glands of the neck enlarged, adherent to one another and caseous. Bronchial glands caseous.

*Larynx and Pharynx* are free from ulceration.

*Stomach and Intestines.* The former is free from tuberculosis, while in the intestine, situated in the patches of Peyer just above the valve, there are several small circumscribed caseous nodules free from ulceration.

*Histological Examination of the Ulcers in the Œsophagus.* The Non-Perforating Ulcer.—The base of this reaches the muscular coat in its central portion and at the edges it gradually merges into the surface of the mucous membrane. The pavement epithelial covering of the mucous membrane can be traced to a point beyond which the infiltration of the tissue extends in the underlying structures. The ulcer has undermined the mucous membrane in this way by the infiltration of the submucous coat, and this has occurred on one side to a greater extent than on the other. About one half of the ulcer is covered by a projecting mass of mucous membrane and submucosa, this overlying mass being covered on its under side by a growth of epithelium which runs along the base of the ulcer for two-thirds of its extent, and is continuous with the surface growth. Some of the mucous glands in the projecting piece of mucous membrane are dilated and filled with cast-off cells and cell detritus. From the fact that the cells are sometimes several layers in thickness in these glands there has doubtless been an active proliferation of epithelium. The veins are dilated, filled with blood, and thick masses of round cells surround them. The arteries show a thickening of their internal coat.

Definite tubercles occur in the base of the ulcer and in the projecting mass of mucous membrane. They are present both in the mucous membrane and in the submucosa, and are composed of epithelioid and lymphoid cells with occasional giant cells. The infiltration, as before stated, extends into the tissues, particularly the submucosa, beyond the ulcer. The tubercles are not caseous, but present evidences of cell necrosis in the presence of fragmentation of nuclei; and leucocytes have been attracted to such areas. Just beneath the new growth of epithelium in the base of the ulcer there are many round, lymphoid cells, and no tubercles.

The muscular coat of the oesophagus in this situation consists of smooth and striped fibers. Tubercles occur in the smooth muscle. The striped fibers often present a swollen, contorted and hyaline aspect, and the nuclei of the sarcolemma are often absent.

The Perforating Ulcer. — The tuberculous process at the edge of the ulcer is found especially in the submucous coat, and it extends below into the muscular coat. Some of the tubercles are quite large, and they are composed principally of epithelioid cells, with an occasional giant cell. The follicles exhibit here also a proliferation and desquamation of cells associated with degeneration of the cast-off ones; and into such follicles leucocytes in considerable numbers have wandered. There has been a partial, but comparatively slight, growth of epithelium along the edge of the ulcer. The muscle in the edges of the ulcer is mostly necrotic and fails to stain, and some fibers present the hyaline metamorphosis.

Tubercle bacilli, although few in number, were found by means of Ziehl's carbol-fuchsin staining method in the tubercles.

Besides the cases given above which represent the most reliable examples of tuberculosis of the oesophagus met with in the literature, there are a number that have been alluded to as doubtful. The most of these have been considered by Weichselbaum, Beck and Zenker and V. Ziemssen, and by common consent rejected. Such are the cases reported by Chovstek, Paulicki and Kraus, and, moreover, two cases which came under Zenker's observation, concerning the interpretation of which he does not commit himself. Finally, those of Uhde and Loeschner, quoted by Penzoldt as tuberculous in character, would seem to belong with the doubtful ones.

However, in examining the cases of Chovstek and Paulicki we think it exceedingly probable that they are examples of tuberculosis. We do not, however, class them with the accepted cases, as no histological examination was made in either instance.

Chovstek's report refers to a man of 43, who eight days before his death began to suffer from difficulty in swallowing. The section, made by Weisbach, revealed tuberculosis of the lungs, and, besides, in the œsophagus, at the level of the 3d dorsal vertebra, numerous losses of substance, some of which were round and others long or irregular in shape. The edges of the ulcers were sharp, but undermined, the bases in part smooth and again irregular. In the base of the ulcers yellowish-white specks were imbedded.

The case of Paulicki occurred in a man of 74 who had tuberculosis of the lungs, larynx and intestines. Three months before his death symptoms of stricture of the œsophagus developed, and at the autopsy a constriction was found at the level of the cricoid cartilage, corresponding with which there was an ulceration of the posterior wall of the œsophagus. The ulcers (two in number) did not reach to the muscular coat, and did not present a caseous appearance. The epiglottis was ulcerated, and characteristic girdle ulcers existed in the intestine.

Again, two of the cases observed by Zenker, and considered as doubtful by him, would appear to belong to our first class and have been given there. The remaining one is stated by him to have occurred in a child. There was a single, round ulcer in the œsophagus, and adjoining this ulcer fine, punctiform nodules were discerned in the mucous membrane. The examination was not conclusive of tuberculosis.

The rarity of this affection and its insidious character probably account for the fact that there is little reference to it in text-books on medicine. It has no definite symptomatology, and the suggestion of Mazzotti that it may be attended with pain, difficulty of swallowing and stricture, while evidently correct, is not distinctive. Penzoldt, however, was able to diagnose during life the third case reported by him, although not until perforation had occurred and the contents of the abscess had been evacuated with the sputum. Hence it may not be out of place to venture the suggestion that great pain on swallowing, or stricture of the œsophagus, developed



during the course of chronic lung and lymph gland tuberculosis or caries of the vertebræ, should be considered with reference to the possible implication of the œsophagus in the tuberculous process.

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